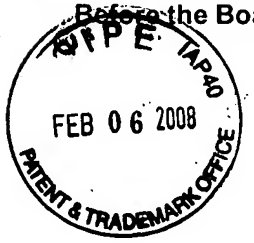
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences



In re Patent Application of

Atty Dkt. GRT-4865-38
C# M#
Confirmation No. 1799

BATTISTINI et al

TC/A.U.: 1614

Serial No. 10/812,308

Examiner: C.E. Rae

Filed: March 30, 2004

Date: February 6, 2008

Title: USE OF (3-(2-ETHYLPHENYL)-5-METHOXYPHENYL)-1H-[1,2,4]-TRIAZOLE FOR THE TREATMENT OF AUTOIMMUNE DISEASES

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

☐ **Correspondence Address Indication Form Attached.**

☐ **NOTICE OF APPEAL**
Applicant hereby **appeals** to the Board of Patent Appeals and Interferences from the last decision of the Examiner twice/finally rejecting applicant's claim(s). $510.00 (1401)/$255.00 (2401) $

☒ An appeal **BRIEF** is attached in the pending appeal of the above-identified application $510.00 (1402)/$255.00 (2402) $ 510.00

☐ Credit for fees paid in prior appeal without decision on merits -$ ( )

☐ A reply brief is attached. **(no fee)**

☒ Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s)
One Month Extension $120.00 (1251)/$60.00 (2251)
Two Month Extensions $460.00 (1252)/$230.00 (2252)
Three Month Extensions $1050.00 (1253/$525.00 (2253)
Four Month Extensions $1640.00 (1254/$820.00 (2254) $

☐ "Small entity" statement attached.

- Less month extension previously paid on -$( )

TOTAL FEE ENCLOSED $ 510.00

☐ **CREDIT CARD PAYMENT FORM ATTACHED.**

Any future submission requiring an extension of time is hereby stated to include a petition for such time extension. The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our **Account No. 14-1140.** A duplicate copy of this sheet is attached.

901 North Glebe Road, 11th Floor
Arlington, Virginia 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100
GRT:ap

NIXON & VANDERHYE P.C.
By Atty: Gary R. Tanigawa, Reg. No. 43,180

Signature: _____

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	Confirmation No. 1799
BATTISTINI et al.	Atty. Ref.: 4865-38
Appln. No. 10/812,308	T.C. / Art Unit: 1614
Filed: March 20, 2004	Examiner: C.E. Rae

FOR: USE OF (3-(2-ETHYLPHENYL)-5-METHOXYPHENYL)-1H-[1,2,4]-TRIAZOLE FOR THE TREATMENT OF AUTOIMMUNE DISEASES

* * *

BRIEF FOR EX PARTE APPEAL

February 6, 2008

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants submit this Brief under 37 CFR § 41.37 to appeal the Examiner's final rejections of claims 9 to 11 as set forth in his Office Action mailed June 6, 2007. The fee required under 37 CFR § 41.20(b)(2) is attached.

Our Notice of Appeal was filed on December 6, 2007 and set February 6, 2008 as the due date for submitting the Brief. Therefore, this Brief is timely filed.

Reversal of the Examiner's claim rejections by the Board of Patent Appeals and Interferences (the "Board") is respectfully requested.

I. REAL PARTY IN INTEREST

The assignee, Sigma-Tu Industrie Farmaceutiche Riunite S.P.A., holds all rights in the subject invention as evidenced by the assignment recorded in the Patent and Trademark Office on October 14, 2004 starting at reel 015890 and frame 0553.

II. RELATED APPEALS AND INTERFERENCES

Appellants, the assignee, and its legal representative do not know of any prior or pending appeal, interference, or judicial proceeding which is related to, directly affects or is directly affected by, or has a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Claims 9-11 are pending. Claims 9-11 stand rejected and are at issue in this appeal. The claims on appeal are set forth in the Claims Appendix.

Claims 1-8 were canceled without prejudice or disclaimer.

IV. STATUS OF AMENDMENTS

An Amendment was submitted under 37 CFR § 1.116 on October 6, 2007. The Examiner did not state in his Advisory Action mailed October 24, 2007 whether or not the amendment would be entered. To clarify the record in view of this omission, the undersigned telephoned the Examiner who promised to consult with his supervisor. No further communication was received.

The amendment to the specification brought the priority claim into conformity with the Examiner's statement that the pending claims were only entitled to an effective filing date of April 15, 2003 and brought the "Summary of the Invention" into conformity with the pending claims. No new matter was introduced by entry of the amendments. Thus, Appellants' amendments did not raise new issues requiring further consideration and placed the application in better form for appeal.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The invention involved in this appeal is directed to treatment of uveitis with 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H-1,2,4-triazole (see pending claim 9). Original claims 1 and 5, page 6 (lines 13-15) of the specification, and pages 13-14 (example entitled "Experimental Autoimmune Uveitis") of the specification support independent claim 9 as presented.

Dependent claims 10-11 are directed to particular embodiments of this invention which specify the subject who is being treated in claim 9. They are supported by original claims 7-8 and page 6 (lines 23-24) of the specification.

Therefore, the invention as presently claimed is clearly supported by Appellants' disclosure as originally filed.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Under 35 U.S.C. 102(b), was it proper to reject claims 9-10 as allegedly anticipated by Mistrello et al. (Immunopharm. 10:163-169, 1985)?

B. Under 35 U.S.C. 103(a), was it proper to reject claim 11 as allegedly unpatentable over Mistrello et al. (Immunopharm. 10:163-169, 1985) in view of Mozes et al. (Clin. Immunol. Immunopharm. 85:28-34, 1997)?

VII. ARGUMENTS

The claims do not stand or fall together because the prior art rejections depend on the citation of different documents. In particular, if the additional citation of Mozes et al. does not justify the Section 103 rejection of claim 11, then the latter would only be objected to as depending from a rejected claim. The issues presented above and separately argued below demonstrate that there are independent bases for patentability and the pending claims should be considered in two groups (1) claims 9-10 and (2) claim 11.

The Examiner acknowledged in the Advisory Action mailed October 24, 2007 that the arguments filed October 6, 2007 overcame the new matter rejection under Section 112, first paragraph (see item 5).

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 9-10 were rejected under Section 102(b) as allegedly being anticipated by Mistrello et al. (Immunopharm. 10:163-169, 1985). Appellants traverse. The cited document does not anticipate the claimed invention because Mistrello et al. fails to teach all of the claim limitations.

Appellants' claimed invention requires "treating uveitis in a subject" by "administering 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H-1,2,4-triazole to said subject." Thus, the compound is administered to a subject and uveitis in the subject is treated by such administration. The Examiner's allegation on page 4 of the Action (i.e., "Mistrello et al. teach the same method step as claimed in the instant application") is plainly incorrect. Uveitis of the "said subject" is treated in claim 1. Nowhere in the Mistrello et al. document is uveitis treated or is the compound administered to a subject having uveitis.

Mistrello et al. disclose that the compound used for treatment in the claimed method has an immunosuppressive effect on antibody responses, delayed type hypersensitivity, and skin graft rejection activity. But there was no effect of the compound on polyarthritis. The compound was taught at page 168 to be "completely ineffective in suppressing adjuvant-induced arthritis" (i.e., polyarthritis). Thus, the effectiveness of the compound against polyarthritis cannot be inherent as alleged on page 4 of the Action because the compound was demonstrated by Mistrello et al. to be completely ineffective under the conditions studied! It is clear that the compound is not universally effective against all autoimmune diseases. Thus, the compound's activities which are disclosed by Mistrello et al. do not teach that the compound would be effective against uveitis.

Claim 1 of Patent No. 6,797,722 (the '722 patent) is directed to the treatment of autoimmune diseases such as multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis with the same compound as the claims in this application. Appellants submit that multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and uveitis all belong to the genus of autoimmune diseases, but each one is a different disease. It is well accepted that a species of a genus does anticipate a different species even if they both belong to the same genus. The disclosure of the '722 patent does not teach that the compound would be effective against uveitis.

Anticipation requires "each and every limitation" to be taught in the same document. Here, the diseases studied by Mistrello et al. do not include uveitis. The cited document attempts to treat polyarthritis, but this disease is not uveitis. Although both polyarthritis and uveitis are autoimmune diseases, they are not the same autoimmune disease. A specific autoimmune disease (e.g., polyarthritis) does not teach a different autoimmune disease (e.g., uveitis). Therefore, to the extent that the Examiner relies on the attempted treatment of polyarthritis in the Mistrello et al. document also to teach treatment of uveitis, Appellants do not agree with this reliance and note that there is no evidence of record that polyarthritis and uveitis are the same disease.

The Kawahito et al. document was cited on pages 4-5 of the Action as "evidence" that the uveitis and polyarthritis treatment groups overlap. But this misunderstands the objectives of the study, its results, and their proper interpretation. Disease susceptibility loci were mapped for collagen-induced arthritis (*Cia*), adjuvant-induced arthritis (*Aia2* and *Aia3*), and experimental autoimmune uveitis (*Eau*). Rats are susceptible or resistant to these autoimmune diseases based on their inheritance of genes mapping to these loci. Inheritance of a disease susceptibility gene increases the *probability* or *chance* that the disease will occur. But there is no strict correlation between possession of a susceptibility gene and occurrence of disease. Fig. 1b shows that there are rats who carry the susceptibility genes and are not affected by adjuvant-induced arthritis (i.e., a maximum arthritis score of 0). Kawahito et al. admit on page 4417 that they have not "definitively demonstrated" that *Aia3*/*Cia3* and *Eau* are allelic. Further even if they were allelic, this would not prove that the diseases are the same. For example, the Examiner appears to acknowledge on page 6 of the Action that adjuvant-induced arthritis (AIA) and collagen-induced arthritis (CIA) are different diseases since they involve different disease mechanisms. At least some of their disease susceptibility genes, however, apparently map to the same loci even though they are different diseases. Thus, mapping of *Aia* and *Eau* disease susceptibility genes to the same genetic interval (i.e., not necessarily allelic) is not sufficient evidence to prove that polyarthritis and uveitis are the same disease.

But inherency may not be established by probabilities or possibilities. *Continental Can v. Monsanto*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) *quoting In re Oelrich*, 212

USPQ 323, 326 (CCPA 1981) ("The mere fact that a certain thing may result from a given set of circumstances is not sufficient"). The extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999) *quoting Continental Can id.* at 1749. Therefore, even if a subject is susceptible to developing both polyarthritis and uveitis, this would merely prove at most that there is a possibility that both diseases are present in the subject (or that a subject treated for polyarthritis would also be treated for uveitis). Both diseases would not necessarily occur in the same subject being treated.

The Mistrello et al. document does not anticipate the claimed invention because it does not disclose all limitations of independent claim 9. Moreover, claims 10-11 depending from the independent claims are also not anticipated by Mistrello et al. because the limitations of claim 9 are incorporated in claims depending therefrom. See *In re McCarn*, 101 USPQ 411, 413 (C.C.P.A. 1954).

Appellants urge the Board to reverse the anticipation rejection because Mistrello et al. fail to disclose all limitations of claims 9 and 10.

35 U.S.C. 103 – Nonobviousness

To establish a case of prima facie obviousness, all of the claim limitations must be taught or suggested by the prior art. See M.P.E.P. § 2143.03. A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing the legal standard provided in *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the

fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning"). Thus, a rejection under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of [prima facie] obviousness is correct." *Kahn*, 78 USPQ2d at 1335; see *KSR*, 82 USPQ2d at 1396. A claim which is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. at 1396. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claim 11 was rejected under Section 103(a) as allegedly being unpatentable over Mistrello et al. (Immunopharm. 10:163-169, 1985) in view of Mozes et al. (Clin. Immunol. Immunopharm. 85:28-34, 1997). Appellants traverse. The combination of Mistrello et al. and Mozes et al. do not render obvious the claimed invention because all claim limitations are not fairly taught or suggested by the cited documents.

Appellants' claimed invention requires "treating uveitis in a [human] subject" by "administering 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H-1,2,4-triazole to said subject." The cited documents fail to teach or suggest treating uveitis in any subject (especially not a human subject). Cf. page 11 of the Action ("Mistrello et al. and Mozes et al. do not teach uveitis"). They also do not teach or suggest treating a human. In contradiction to acceptable principles of logic and causality, the Examiner alleges on pages 7-8 that the ineffectiveness of the compound in treating polyarthritis at doses of 2 mg/kg/day would allow a skilled artisan to "reasonably envision that the administration of an identical dose of DLT111-IT to subjects suffering from uveitis and polyarthritis would necessarily effectuate an immunosuppressive effect in treating both uveitis and polyarthritis." It makes no sense whatsoever that the failure to effectively treat polyarthritis according to the teachings of the Mistrello et al. document would bolster an argument of a reasonable expectation of success to treat uveitis using the immunosuppressive activity of the compound! It certainly would not provide "a reasonable expectation of success that DL111-IT would exhibit immunosuppressive activity in humans suffering from uveitis."

Cf. page 11 of the Action. No evidence or reasoning is provided in the Action for extrapolating from the combination of Mistrello et al. and Mozes et al. when neither document teaches or suggests (i) treating uveitis and (ii) treating a human.

In the Mistrello et al. document, the compound was shown not to be effective in treating polyarthritis. One of ordinary skill in the art would have understood from their negative result that there was no reasonable expectation of success to use the recited compound as an immunosuppressive agent in treating any autoimmune disease, which includes uveitis. Therefore, there is no reasonable expectation of success provided in Mistrello et al. or in any other evidence of record. But a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rhinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976). Moreover, the requirements of M.P.E.P. § 2144.08 are not satisfied for establishing a case of prima facie obviousness in accordance with the guidelines for the examination of claims directed to a species when the reference discloses the genus. Here, Mistrello et al. and Mozes et al. fail to disclose successful treatment of any autoimmune disease in a human or any other subject.

Appellants urge the Board to reverse the obviousness rejection because one of ordinary skill in the art would not have found claim 11 to be obvious over the combination of Mistrello et al. and Mozes et al. at the time the invention was made.

Conclusion

For the reasons discussed above, the Examiner's rejections are improper and they should be reversed by the Board. Appellants submit that the pending claims are in condition for allowance and earnestly solicit an early Notice to that effect.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

Gary R. Tanigawa
Reg. No. 43,180

901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

VIII. CLAIMS APPENDIX

9. A method for treating uveitis in a subject in need thereof, comprising administering 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H-1,2,4-triazole to said subject.

10. The method of claim 9, wherein said subject is a mammal.

11. The method according to claim 9, wherein said subject is a human.

IX. EVIDENCE APPENDIX

None.

X. RELATED PROCEEDINGS APPENDIX

None.